

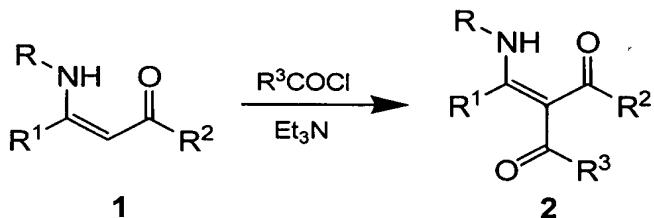
## REMARKS

Applicants have canceled Claim 10 as being drawn to non-elected subject matter. Applicants again reserve the right to file one or more divisional applications directed to all non-elected subject matter.

### Rejection under 35 U.S.C. 103

Claims 8-9 stand rejected under 35 U.S.C. 103(a) as being unpatentable over the cited Angelov article (in *Synthesis* 14, 2221-2225 (2003)) in view of U.S. Patent 6,388,124 ("Takahashi et al"). Applicants respectfully traverse.

As fully discussed in their previous Amendment dated April 26, 2007, Angelov discloses acylation of enaminones of formula **1** to form compounds of formula **2** as shown in the following reaction scheme taken from page 2222 of the reference:



in which the various groups can apparently have various meanings but are defined in a very limited manner to include embodiments in which **R** is one of a few specific lower alkyl or optionally ring-substituted benzyl or phenethyl; **R**<sup>1</sup> is methyl or phenyl; **R**<sup>2</sup> is methyl, ethoxy, amino, anilino, or diethylamino; and **R**<sup>3</sup> is methyl,  $\text{CCl}_3$ , or optionally substituted phenyl. As noted in the Final Office Action at page 4, Angelov teaches that compounds of formula **1** having the specific substituents shown for formulas **1a-h** can be acylated in the presence of bases such as  $\text{Et}_3\text{N}$  or pyridine to form compounds of formula **2** and further teaches that the additional compounds of formulas **2i-p** can similarly be obtained. See page 2222, bottom of left column. The only halogenated compounds disclosed in Angelov are those in which **R**<sup>3</sup> is limited to trichloromethyl. However, Applicants again point out that Angelov does not disclose corresponding dichloromethyl compounds. As will be discussed in detail below, Applicants maintain that this difference is a critical feature of their claimed invention.

Applicants note at the outset that nothing in Angelov even remotely suggests inorganic aqueous bases. Consequently, Applicants' invention could not be rendered obvious to the extent that the base can be an inorganic aqueous base. Applicants

also maintain that their invention is also not obvious as it relates to the other specified bases.

Even without reliance on Takahashi et al, the Final Office Action at page 4 states that "the chloromethyl end of the acyl halide is not involved in the chemistry of the reactions, and there is no evidence that it is less stable under these reaction conditions than a dichloromethyl substituted acyl halide" and concludes that Angelov, both by itself and taken with Takahashi et al, teaches the equivalency of triethylamine and pyridine and other nitrogenous bases. Applicants respectfully submit that these conclusions are incorrect for at least two reasons.

First, the Final Office Action has apparently failed to take into account the known instability of dihaloacyl groups in the presence of triethylamine. This problem is discussed in Applicants' specification at page 1, lines 20-25. The specification first refers to WO 03/051820 (which corresponds to U.S. Patent 6,706,911, previously provided by Applicants), which discloses the preparation of 2-perhaloacyl-3-amino-acrylic acid derivatives by reaction of 3-aminoacrylic esters with perhaloalkyl-carboxylic anhydrides in the presence of bases such as tertiary nitrogen bases. E.g., column 1, lines 37-47 (generally), and column 3, lines 33 et seq (the bases). Here, none of the halogenated reactants has a  $(\text{Hal})_2\text{CH}-$  group. As explained in Applicants' specification, the disclosed process would be "unsuitable for preparing dihaloacyl-substituted aminoacrylic acid derivatives, since hydrogen chloride is eliminated in the presence of triethylamine when there is an  $\alpha$ -hydrogen" (emphasis added) to form dihaloketenes that are very unstable and subject to polymerization (as discussed in *J. Org. Chem.* 1968, 33, 816). If triethylamine and pyridine are considered equivalent (or even only interchangeable) as proposed in the Final Office Action, those skilled in the art aware of this art would have expected poor if any yields and purity for dihalomethyl-substituted compounds. Applicants, in contrast, obtained impressive yields or pure products when their claimed process was used. Applicants therefore respectfully submit that those skilled in the art would not have been led by Angelov to their claimed invention.

Second (and even if the preceding paragraph were ignored), Applicants submit that the only thing that Angelov teaches is that the nitrogenous bases at issue might be interchangeable – which is not the same as teaching their equivalence – but only when the disclosed reactions are carried out with the disclosed enaminones

of formula 1 to form the disclosed compounds of formula 2. Applicants maintain that Takahashi et al does not bridge the gap between Angelov and their claimed invention. Takahashi et al discloses a completely different reaction of completely different reactants than what Applicants claim. As previously discussed, Takahashi et al teaches the halogenation of alcohol reactants to form corresponding halogen-substituted compounds by conversion of C-OH groups to C-Cl groups using a halogenating agent, whereas Applicants' claimed process – as well as the process disclosed in Angelov – is directed to acylation of an enaminone moiety to form a dicarbonyl moiety. The reactions are mechanistically so dissimilar that those skilled would simply not rely on Takahashi et al to teach the equivalency – or otherwise – of triethylamine and pyridine derivatives for reactions other than the type it discloses. Applicants maintain that Takahashi et al is completely irrelevant to their claimed acylation process. Even if some inference could be drawn from the teachings of Takahashi et al, Applicants again point to the unexpected advantages obtained by using pyridine or pyridine derivatives instead of tertiary amines such as triethylamine. These unexpected advantages are discussed generally in their specification (e.g., at page 3) and are supported specifically by experimental data in the examples showing that 2-methyl-5-ethylpyridine and other pyridines provide superior results compared to triethylamine. Although the Final Office Action refers to the high yields disclosed in Angelov, such results are restricted to compounds that do not contain the problematic dihalomethyl groups discussed above and cannot properly be extended to compounds containing dihalomethyl groups.

Applicants therefore respectfully maintain that their claims as amended are not rendered obvious by the Angelov article in view of Takahashi et al.

In view of the preceding amendments and remarks, allowance of the claims is respectfully requested.

Respectfully submitted,

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